Please add the following new Claims 16-17:

16. (New) The method of Claim 9, wherein said nucleic acid expressing said protein comprises:

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.

17. (New) The method of Claim 9, wherein said nucleic acid expressing said protein comprises an expression plasmid comprising:

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.

REMARKS

***The Amendments*:**

Claims 1-7 and 10-15 have been canceled, without prejudice. New Claims 16 and 17 have been added. The new claims do not introduce new matter and are fully supported by the specification of the present application and the claims as originally filed. Therefore, entry of the amendments under 37 C.F.R. § 1,111 is respectfully requested. A marked-up version of the amended claims is attached hereto as *Appendix B*. The Claims as pending are attached hereto as *Appendix C*.

The specification has been amended to add the SEQ ID Nos. at the appropriate places. FIGURE 1 has been replaced by FIGURES 1A and 1B in order to conform with the rules of practice, and further has been amended to correct a typographical error (*i.e.*, the character "<" between nucleotide positions 537 and 538 has been removed). These amendments to the specification and to FIGURE 1 do not introduce new matter, and they are fully supported by the specification and FIGURE 1 as originally filed.

***Response to Restriction Requirement*:**

In response to the Restriction Requirement, Applicants hereby elect Group V, encompassing Claims 8 and 9, which are drawn to a method for the negative regulation of the keratinization of hair comprising administering a therapeutically effective amount of a protease-related protein, with traverse. Applicants respectfully request, however, reconsideration of the restriction requirement and its modification to combine the claims of Group VI covering a method for the negative regulation of the keratinization of hair comprising administering a therapeutically effective amount of a protease-related protein as recited in Claims 8 and 9 (*i.e.*, Group V) along with additional substances which inhibit the proteins Ha3 and/or CK15 (Claims 10 and 11) with the claims of Group V. Applicants submit that the subject matter of the claims of Groups V and VI is so inextricably intertwined so as to merit examination in one application, related as they are, as claims reciting a method administering the compounds of the invention, and *dependent* claims directed to the same methods administering one or more additional substances. Applicants urge further that examination of the claims of Groups V and VI would not require an additional search.

Applicants request that the elected claims be examined in this application, along with Claims 16 and 17 added by the amendments made herein.

Response to Species Election Requirement.

In response to the species election requirement, Applicants elect for immediate examination the protease related protein. All elected claims read on this species.

CONCLUSION

No fee is believed to be due with this response. However, if it is determined that fees are due, please charge them to Pennie & Edmonds LLP Deposit Account No. 16-1150. A copy of this sheet is enclosed for accounting purposes (order no. 8484-081-999).

Respectfully submitted,

Date 12 September 2001

43,341

Birgit Millauer (Reg. No.)

for: Laura A. Coruzzi (Reg. No. 30,742)

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Enclosures

APPENDIX A
Marked Up Versions of Amended Paragraphs:

Please replace Figure 1 with the enclosed revised Figure 1.

On page 2, please replace the paragraph beginning "FIGURE 1 shows the base sequence of a cDNA..." with the following paragraph:

--[FIGURE 1] FIGURES 1A and 1B shows the base sequence of a cDNA (SEQ ID NO: 1) according to the invention as well as the amino acid sequence (SEQ ID NO: 2) derived therefrom, of a (PVP) according to the invention.--

On page 2, please replace the paragraph beginning "Thus, the subject matter of the present invention..." with the following paragraph:

--Thus, the subject matter of the present invention is represented by a protease-related protein, the protein comprising the amino acid sequence of [FIGURE 1] FIGURES 1A and 1B (SEQ ID NO:2) or an amino acid sequence differing therefrom by one or more amino acids.--

On page 2, please replace the paragraph beginning "The third gene codes for a protein which has homologies..." with the following paragraph:

--The third gene codes for a protein which has homologies with respect to a protease of the kallikrein family, optionally a protease activity, but differs from a known protease of the kallikrein family on the DNA level by hybridization under normal conditions. Such a protein has the amino acid sequence of [FIGURE 1] FIGURES 1A and 1B (SEQ ID NO:2) or an amino acid sequence differing therefrom by one or more amino acids. Furthermore, the applicant has found that when the gene product of the whn gene is lacking the genes of Ha3 and CK15 are underexpressed whereas the gene of the above protein is overexpressed.--

On page 2, please replace the paragraph beginning "(a) the DNA of FIGURE 1 or a DNA differing therefrom by one or more base pairs..." with the following paragraph:

--(a) the DNA of [FIGURE 1] FIGURES 1A and 1B (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs,

(b) a DNA hybridizing with the DNA of (a), or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.--

On page 3, please replace the paragraph beginning "A section of the DNA of FIGURE 1 was deposited..." with the following paragraph:

--A section of the DNA of [FIGURE 1] FIGURES 1A and 1B (SEQ ID NO: 1) was deposited with the DSMZ (*Deutsche Sammlung von Mikroorganismen und Zellkulturen* [German-type collection of microorganisms and cell cultures]) as pRDA2-1a under DSM 11522 on April 23, 1997.--

On page 6, please replace the paragraph beginning " The following oligonucleotide adaptor pairs were required for the RDA..." with the following paragraph:

--The following oligonucleotide adaptor pairs were required for the RDA:

R-Bgl -12: 5' -GATCTGCGGTGA- 3'(SEQ ID NO: 3)

R-Bgl -24: 5' -AGCACTCTCCAGCCTCTCACCGCA -3' (SEQ ID NO: 4)

R-Bgl -12: 5' -GATCTGTTCATG -3' (SEQ ID NO: 5)

R-Bgl -24: 5' -ACCGACGTCGACTATCCATGAACA -3' (SEQ ID NO: 6)

N-Bgl -12: 5' -GATCTTCCCTCG -3' (SEQ ID NO: 7)

N-Bgl -24: 5' -AGGCAACTGTGCTATCCGAGGGAA -3' (SEQ ID NO: 8).--

On page 16, please replace the paragraph beginning "Thereafter, those DNA fragments which proved to be "real" difference products..." with the following paragraph:

--Thereafter, those DNA fragments which proved to be "real" difference products in the Southern analysis, were investigated by means of Northern hybridizations: RNAs from the investigated tissues (whn(+/+) skin-cDNA and nu/nu skin-cDNA) were blotted and hybridized with the radioactively labeled cloning products. By this, the differential expression of these sequences was confirmed in the investigated tissues. An analysis of the sequences yielded the cDNA of [FIGURE 1] FIGURES 1A and 1B (SEQ ID NO: 1) according to the invention.--

On page 16, please replace the paragraph beginning "For the preparation of a (PVP) according to the invention..." with the following paragraph:

--For the preparation of a (PVP) according to the invention, the vector pBSNot-PVP of Example 1 is cleaved by BamHI, the DNA coding for (PVP) is isolated and inserted in the expression vector pQE-8 (Quiagen company) cleaved by BamHI. The expression plasmid pQ/PVP is obtained. Such a plasmid codes for a fusion protein comprising 6 histidine residues (N terminus partner) and the (PVP) of [FIGURE 1] FIGURES 1 A and 1B (SEQ ID NO: 2) according to the invention (C terminus partner). pQ/PVP is used for transforming *E. coli* SG 13009 (Gottesman *et al.*, 1981, *J. Bacteriol.* 148:265-273) . The bacteria are cultivated in an LB broth with 100 μg/ml ampicillin and 25 μg/ml kanamycin and induced with 60 μM isopropyl-1β-D-thiogalactopyranoside (IPTG) for 4 h. The addition of 6 M guanidine hydrochloride serves for achieving lysis of the bacteria, thereafter a chromatography (Ni-NTA resin) is carried out with the lysate in the presence of 8 M urea corresponding to the instructions of the manufacturer (Quiagen

company) of the chromatography material. The bound fusion protein is eluted in a buffer having pH 3.5. After its neutralization, the fusion protein is subjected to an 18 % SDS-polyacrylamide gel electrophoresis and dyed with Coomassie blue (Thomas and Kornberg, 1975, *J. Mol. Biol.* 149:709-733). In this way, a (fusion) protein according to the invention can be prepared in highly pure form.--

APPENDIX B

MARKED-UP COPY OF AMENDED CLAIMS

8. (Amended) A method for the negative regulation of the keratinization of hair, comprising administering [the protein of Claim 1] in a therapeutically effective amount a protease-related protein, said protein comprising the amino acid sequence of (SEQ ID NO: 2) or an amino acid sequence differing therefrom by one or more amino acids.

--16. (New) The method of Claim 9, wherein said nucleic acid expressing said protein comprises:

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.

17. (New) The method of Claim 9, wherein said nucleic acid expressing said protein comprises an expression plasmid comprising :

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.--

APPENDIX C

CLAIMS AS PENDING AFTER THE RESTRICTION AND INSTANT AMENDMENT

1. A protease-related protein, said protein comprising the amino acid sequence of FIGURE 1 or an amino acid sequence differing therefrom by one or more amino acids.

2. A DNA encoding the protein of Claim 1, wherein the DNA comprises:
   (a) the DNA of FIGURE 1 or a DNA differing therefrom by one or more base pairs,
   (b) a DNA hybridizing with the DNA of (a), or
   (c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.

3. An expression plasmid comprising the DNA of Claim 2.

4. A transformant comprising the expression plasmid of Claim 3.

5. A process for the preparation of the protein of Claim 1, comprising the cultivation of the transformant of Claim 4 under suitable conditions.

6. An antibody directed against the protein of Claim 1.

7. A method for detecting the keratinization of hair, comprising application the protein of Claim 1, the DNA of Claim 2, or the antibody of Claim 6.

8. A method for the negative regulation of the keratinization of hair, comprising administering in a therapeutically effective amount a protease-related protein, said protein comprising the amino acid sequence of (SEQ ID NO: 2) or an amino acid sequence differing therefrom by one or more amino acids.

9. The method of Claim 8, wherein the protein is present as such or in the form of a nucleic acid expressing it.

10. The method of Claim 8 or 9, wherein additionally substances are administered which inhibit the proteins Ha3 and/or CK15.

11. The method of Claim 10, wherein the substances are antibodies directed against Ha3 and CK15, respectively, and/or anti-sense oligonucleotides, all of which inhibit the expression of the nucleic acids encoding these proteins.

12. A method for the positive regulation of the certification of hair, comprising administering the protein of Claim 1.

13. The method of Claim 12, wherein the protein is present in the form of a substance inhibiting it.

14. The method of Claim 13, wherein the substance is an antibody of Claim 6 and/or an anti-sense oligonucleotide which inhibits the expression of the nucleic acid encoding the protein.

15. The method of Claim 12, 13, or 14, wherein the proteins Ha3 and/or CK15 are also present as such or in the form of nucleic acids expressing them.

16. The method of Claim 9, wherein said nucleic acid expressing said protein comprises:

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.

17. The method of Claim 9, wherein said nucleic acid expressing said protein comprises an expression plasmid comprising :

(a) the DNA of (SEQ ID NO: 1) or a DNA differing therefrom by one or more base pairs;

(b) a DNA hybridizing with the complement of the DNA of (a); or

(c) a DNA related to the DNA of (a) or (b) via the degenerated genetic code.